Synthesis of 3-acetyl-N-aryl-4-diethylaminoselenet-2(2H)-imines from 4-diethylamino-3-butyn-2-one and aryl isoselenocyanates

Atanassov, Plamen K ; Linden, Anthony ; Heimgartner, Heinz

Abstract: The reaction of aryl isoselenocyanates (1a-d) with 4-diethylamino-3-butyn-2-one (6) in refluxing tetrahydrofuran afforded N-arylselenet-2(2H)-imines (7) in moderate yields. The structure of the stable 4-bromophenyl derivative (7b) has been established by X-Ray crystallography. A stepwise cycloaddition via an intermediate zwitterion (A/A¢) is proposed as the reaction mechanism. In boiling tetrahydrofuran, the selenetimines (7) are in equilibrium with ketenimines (B), which were intercepted by amines to give 2-(diaminomethylene)-3-oxobutane selenamides of type (8).

HETEROCYCLES, Vol. 62, 2004, pp. 521 - 533
Received, 1st August, 2003, Accepted, 3rd October, 2003, Published online, 7th November, 2003

SYNTHESIS OF 3-ACETYL-*N*-ARYL-4-DIETHYLAMINO-SELENET-2(2*H*)-IMINES FROM 4-DIETHYLAMINO-3-BUTYN-2-ONE AND ARYL ISOSELENOCYANATES

Plamen K. Atanassov,[1] Anthony Linden, and Heinz Heimgartner*

Institute of Organic Chemistry, University of Zürich, Winterthurerstrasse 190, CH-8057 Zürich, Switzerland; E-mail: heimgart@oci.unizh.ch

Dedicated to Professor Leo A. Paquette at the occasion of his 70th birthday

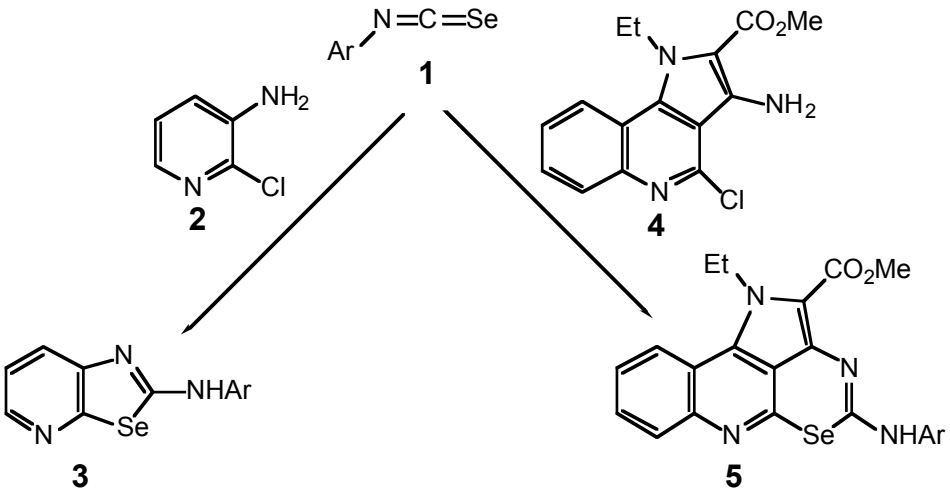
Abstract – The reaction of aryl isoselenocyanates (**1a-d**) with 4-diethyl-amino-3-butyn-2-one (**6**) in refluxing tetrahydrofuran afforded *N*-arylselenet-2(2*H*)-imines (**7**) in moderate yields. The structure of the stable 4-bromophenyl derivative (**7b**) has been established by X-Ray crystallography. A stepwise cycloaddition *via* an intermediate zwitterion (**A**/**A′**) is proposed as the reaction mechanism. In boiling tetrahydrofuran, the selenetimines (**7**) are in equilibrium with ketenimines (**B**), which were intercepted by amines to give 2-(diaminomethylene)-3-oxobutane selenamides of type (**8**).

INTRODUCTION

In the last few years, the attractivity of selenaheterocycles has increased remarkably because of their interesting reactivities[1] and pharmaceutical applications[2] (see also lit. cited in ref.[3]). As many syntheses of selenium-containing heterocycles involve the use of toxic selenium reagents, which are often difficult to handle, new synthetic approaches are of high interest. Recently, we have shown that isoselenocyanates are convenient precursors for the introduction of selenium into heterocycles.[3-6] They are easy and relatively cheap to prepare, safe to handle, and less

toxic. For example, aryl isoselenocyanates (**1**) react with 3-amino-2-chloropyridine (**2**) to give selenazolo[5,4-*b*]pyridines (**3**),[3] and with the 2-chloroquinoline derivative (**4**), 1*H*-1,3,6-triazaaceanthrylenes of type (**5**) are obtained (*Scheme 1*).

Scheme 1



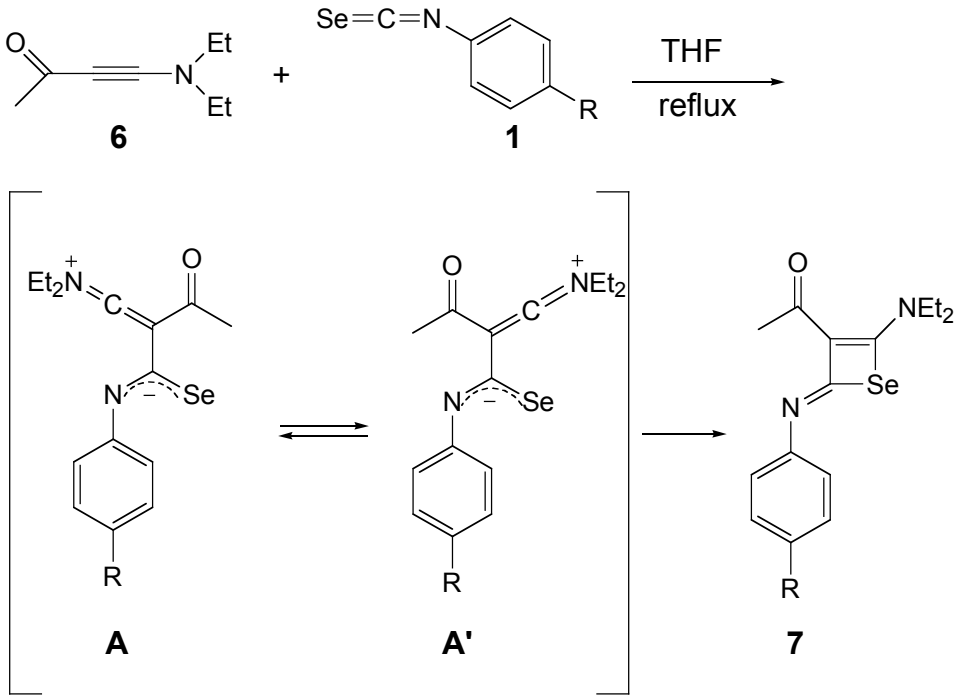
Recently, *Yoo et al*. reported on the reaction of isothiocyanates with ynamines, which led to four-membered thiet-2(2*H*)-imines *via* a formal [2 + 2] cycloadditon.[7] With the aim of preparing the analogous selenaheterocycles, we investigated the reaction of 4-diethylamino-3-butyn-2-one (**6**) with aryl isoselenocyanates (**1**).

RESULTS AND DISCUSSION

Heating of a solution of equimolar amounts of aryl isoselenocyanates (**1a**-**d**) and 4-diethyl-amino-3-butyn-2-one (**6**) in tetrahydrofuran (THF) under reflux led to the disappearance of **1** within two hours (TLC). Evaporation of the solvent and treatment of the oily residue with a mixture of ethyl acetate, petroleum ether, and methanol gave yellowish crystalline solids, which were identified as 3-acetyl-*N*-aryl-4-diethylaminoselenet-2(2*H*)-imines (**7a**-**c**) (*Scheme 2*) on the basis of their elemental analyses and spectroscopic data. For example, **7b** shows strong IR absorptions (KBr) at 1703, 1629, and 1564 cm^{-1} for C=O, C=N, and C=C bonds, respectively. In the ^{1}H-NMR spectrum ($CDCl_3$), the diethylamino group absorbs as two broad signals for two CH_2N (4.27 and 3.38 ppm) and a triplet at 1.31 ppm (J = 7.1 Hz) for two Me groups. In the ^{13}C-NMR spectrum, the C=O group appears at 186.1 ppm, which is characteristic of a vinylogous

amide structure. The sp^2-C atoms of the four-membered ring (C(2)-C(4)) absorb as singlets between 161.1 and 112.5 ppm together with the C-atoms of the benzene ring. Again, the CH_2N groups of the diethylamino residue show two triplets at 53.5 and 49.3 ppm, whereas the two Me groups absorb as a quartet at 14.2 ppm. In the case of the 4-methoxyphenyl derivative (**7d**), the product could not be crystallized and remained as an intractable glue.

Scheme 2



a R = H, **b** R = Br, **c** R = Cl, **d** R = MeO

Finally, the structure of the selenet-2(2*H*)-imine (**7b**) was established unambiguously by X-Ray crystallography (*Figure 1*). The selenete ring is almost planar, and the attached atoms N(2), N(4), and C(11) deviate only slightly from this plane. Furthermore, the acetyl group at C(3) is almost coplanar with the heterocycle (dihedral angle C(4)-C(3)-C(11)-O(11) 8.5(4)°), whereas the benzene ring is twisted out of this plane (dihedral angle C(2)-N(2)-C(5)-C(6) –49.6(3)°). The bond lengths involving atoms C(2), C(3), C(4), N(4), and C(11) show a significant π-electron delocalization in this region of the molecule. One of the *N*-ethyl groups is disordered over two conformations with the major conformation I being present in about 71% of the molecules. In the

major conformation, the diethylamino group is also coplanar with the core heterocycle (dihedral angles Se(1)-C(4)-N(4)-C(13a) –178.5(2)° and C(3)-C(4)-N(4)-C(15) –177.0(3)°).

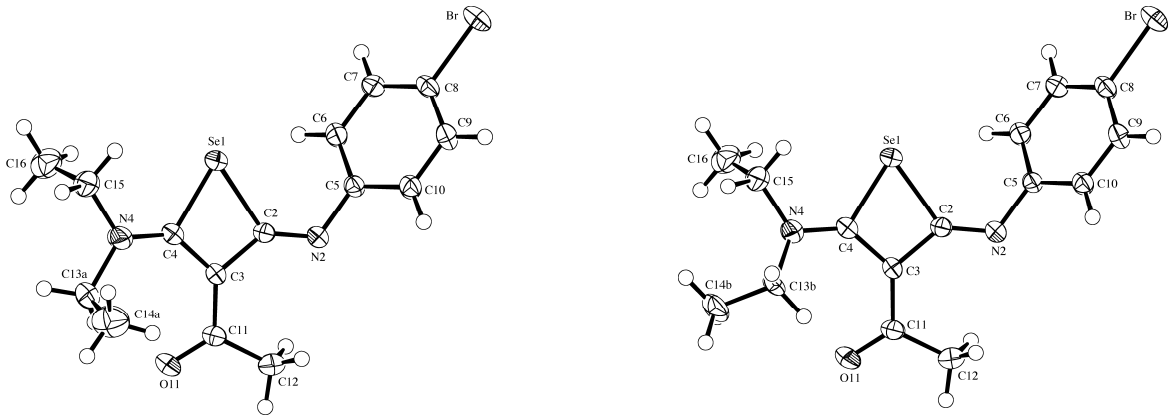


Figure 1. ORTEP plot[8] of the molecular structure of the two conformations **I** (left, 71%) and **II** (right, 29%) of **7b** (arbitrary numbering of atoms; 50% probability ellipsoids).

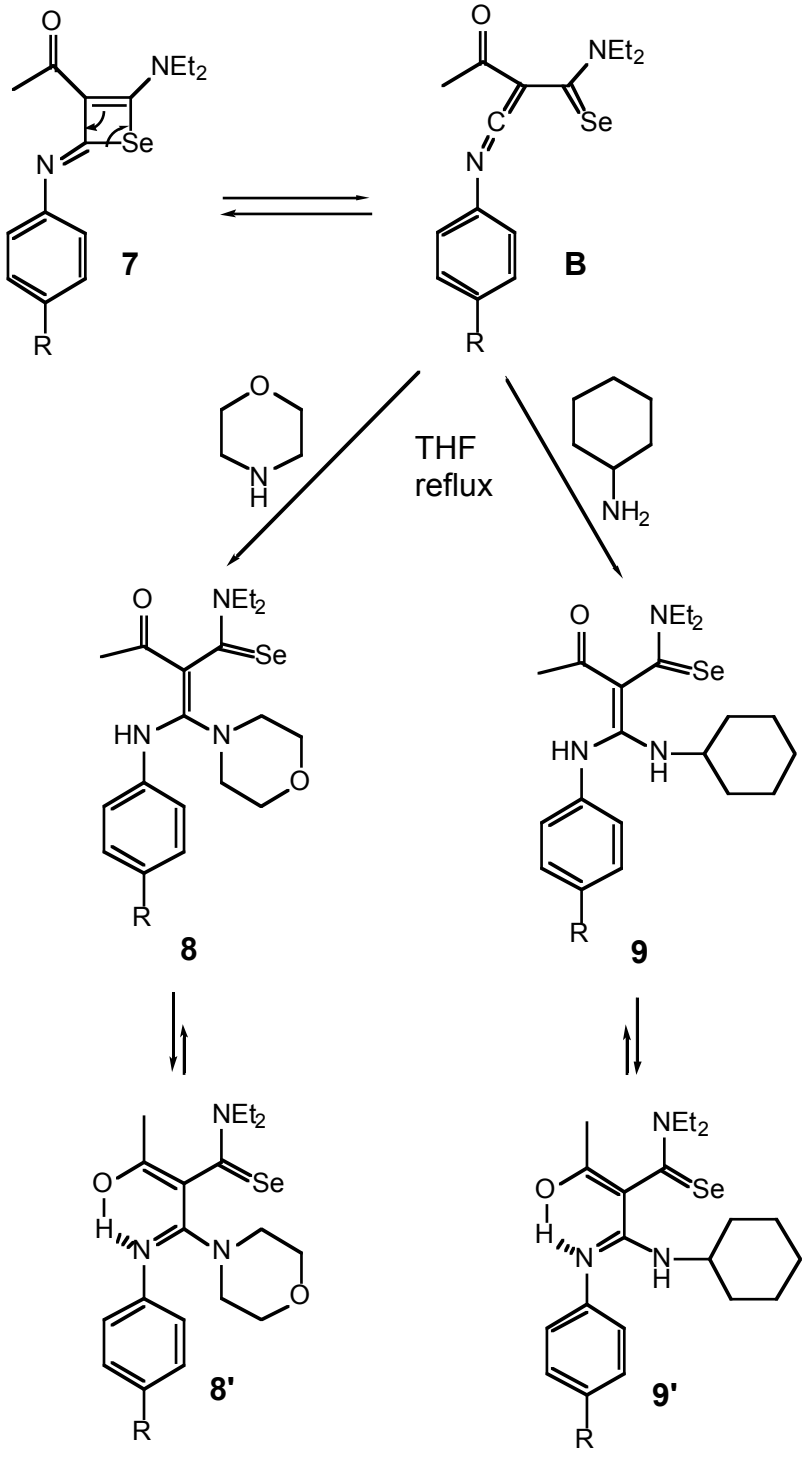
The selenet-2(2*H*)-imines (**7**) are formal [2+2] cycloadducts of the starting materials (**1**) and (**6**), but it is most likely that they are formed by a two-step mechanism (cf. also ref.[7]). The push-pull substituted alkyne (**6**) undergoes a nucleophilic addition onto the isoselenocyanate (**1**) to give a zwitterionic intermediate of type **A**/**A′** (*Scheme 2*). Ring closure between the Se atom and the keteniminium moiety leads to the formation of the selenete ring.

When solutions of **7** in THF were treated with morpholine or cyclohexylamine at reflux temperature, 2-diaminomethylene-3-oxobutane selenamides (**8**) and (**9**), respectively, were obtained in moderate yields (*Scheme 3*). In the case of the 4-methoxyphenyl derivative (**7d**), the crude material obtained from the reaction between **1d** and **6** was used directly. The structures of the 1:1 adducts are supported by elemental analyses, mass spectra, and ^{13}C-NMR spectra. Surprisingly, the IR spectra (KBr) do not show a C=O absorption, indicating that the products exist in an enolized form, *e.g.* **8′** and **9′**. In the ^{1}H-NMR spectrum, the singlet at *ca.* 14.5 ppm is in agreement with an enol structure involved in an intramolecular hydrogen bond.

A reaction mechanism for the formation of **8** and **9** is proposed in *Scheme 3*. Electrocyclic ring opening of the selenetes (**7**) leads to the ketenimines of type **B**. Then, nucleophilic addition of

amines with these reactive intermediates gives the observed adducts, for which several enol structures are conceivable.

Scheme 3



a R = H, **b** R = Br, **d** R = MeO

In conclusion, we have shown that aryl isoselenocyanates (**1**) undergo a formal [2+2] cycloaddition with the ynamine (**6**) to give selenet-2(2*H*)-imines (**7**) in analogy to the reaction involving isothiocyanates, which leads to the corresponding thiet-2(2*H*)-imines.[7]

EXPERIMENTAL

General remarks. See ref.[5a] IR spectra in KBr (cm^{-1}), NMR spectra at 300 (^1H) and 75.6 (^{13}C) MHz in $CDCl_3$ (ppm), and CI-MS with NH_3 (*m/z* (rel.%)).

Starting materials. The aryl isoselenocyanates (**1a-d**) were prepared according to the protocol described in ref.[8] To a stirred solution of the corresponding *N*-arylformamide (40 mmol) in dry toluene (100 mL) in an ice bath, Et_3N (16.2 g, 160 mmol) and Se black powder were added. Then, phosgene (30 g of a 20% solution in toluene, 60 mmol) was added slowly within 30 min. An exothermic reaction took place. After complete addition, the suspension was heated under reflux for 8-10 h (TLC control). The mixture was filtered and washed with several portions of toluene, the filtrate was concentrated and fractionated (SiO_2 column) using hexane as the eluent. Phenyl isoselenocyanate (**1a**):[8] 4.84 g (40 mmol) of *N*-phenylformamide; yield: 3.24 g (45%). 4-Bromophenyl isoselenocyanate (**1b**): 8.00 g (40 mmol) of *N*-(4-bromophenyl)-formamide; yield: 6.05 g (58%). 4-Chlorophenyl isoselenocyanate (**1c**):[8] 6.22 g (40 mmol) of *N*-(4-chlorophenyl)formamide; yield: 4.77 g (55%). 4-Methoxyphenyl isoselenocyanate (**1d**):[8] 6.05 g (40 mmol) of *N*-(4-methoxyphenyl)formamide; yield: 3.56 g (42%). *N*-(4-Chlorophenyl)- and *N*-(4-bromophenyl)formamide were prepared according to ref.[9] by heating the corresponding aniline (20 mmol) in 95% formic acid under reflux for 30 min. After workup, the products were recrystallized from H_2O. *N*-(4-Methoxyphenyl)formamide was prepared analogously according to ref.[10] After evaporation of the solvent, the residue was dissolved in AcOEt and the solution was washed with 5% aq. $NaHCO_3$ and H_2O. The organic layer was dried ($MgSO_4$), the solvent evaporated, and the crude product was used without further purification. 4-Diethylamino-3-butyn-2-one (**6**) was synthesized following the protocol in ref.[11]

Synthesis of selenet-2(2*H*)-imines. General procedure. To a stirred solution of 4-diethylamino-3-butyn-2-one (**6**) in dry THF under argon, an equimolar amount of the respective aryl isoselenocyanate was added, and the mixture was stirred for 2 h under reflux. After cooling

to rt, the solvent was evaporated under vacuum, and the remaining oil was treated with AcOEt/petroleum ether/MeOH. After cooling in an ice bath, yellowish crystals formed within 3 h.

3-Acetyl-4-diethylamino-N-*phenylselenet-2(2*H)*-imine* (**7a**). From 0.44 g (3.2 mmol) of **6** and 0.60 g (3.3 mmol) of phenyl isoselenocyanate (**1a**): 0.41 g (41.6%). Yellowish crystals; mp 104-105°C (AcOEt/pet. ether/MeOH). IR: 3065*w*, 3000*m*, 2972*s*, 2929*m*, 1706*s*, 1631*s*, 1592*s*, 1558*s*, 1483*m*, 1460*m*, 1442*m*, 1391*s*, 1356*s*, 1256*m*, 1201*w*, 1188*w*, 1168*m*, 1157*m*, 1108*w*, 1092*m*, 1072*m*, 1020*m*. ^{1}H-NMR: 7.36-7.00 (*m*, 5 arom. H); 4.27, 3.38 (2 br *s*, 2 CH_2N); 2.50 (*s*, MeCO); 1.31 (*t*, *J* = 7.1, 2 Me). ^{13}C-NMR: 186.0 (*s*, CO); 161.6, 149.4, 140.1, 112.6 (4*s*, 1 arom. C, C(2), C(3), C(4)); 129.1, 125.0, 121.1 (3*d*, 5 arom. CH); 53.0, 49.3 (2 br, 2 CH_2N); 31.2 (*q*, *Me*CO); 14.2 (*q*, 2 Me). CI-MS: 323 (100, $[M+1]^+$). Anal. Calcd for $C_{15}H_{18}N_2OSe$: C, 56.08; H, 5.65; N, 8.72. Found: C, 56.04; H, 5.81: N, 8.70.

3-Acetyl-N-*(4-bromophenyl)-4-diethylaminoselenet-2(2*H*)-imine* (**7b**). From 0.19 g (1.4 mmol) of **6** and 0.37 g (1.4 mmol) of 4-bromophenyl isoselenocyanate (**1b**): 0.40 g (71.4%). Yellowish crystals; mp 105-107°C (AcOEt/pet. ether/MeOH). IR: 2973*m*, 2932*m*, 1703*s*, 1629*s*, 1564*s*, 1478*s*, 1460*m*, 1443*m*, 1390*s*, 1305*m*, 1258*m*, 1186*m*, 1162*m*, 1092*m*, 1070*m*, 1018*w*, 1008*m*. ^{1}H-NMR: 7.43, 6.90 (*AA'BB'*, *J* = 8.7, 4 arom. *H*); 4.27, 3.38 (2 br *s*, 2 CH_2N); 2.47 (*s*, MeCO); 1.31 (*t*, *J* = 7.1, 2 Me). ^{13}C-NMR: 186.1 (*s*, CO); 161.1, 148.5, 140.7, 118.3, 112.5 (5*s*, 2 arom. C, C(2), C(3), C(4)); 132.2, 122.8 (2*d*, 4 arom. CH); 53.5, 49.3 (2 br, 2 CH_2N); 31.2 (*q*, *Me*CO); 14.2 (*q*, 2 Me). CI-MS: 401(100, $[M+1]^+$). Anal. Calcd for $C_{15}H_{17}N_2OBrSe$: C, 45.02; H, 4.28; N, 7.00. Found: C, 45.08; H, 4.35; N, 6.99.

3-Acetyl-N-*(4-chlorophenyl)-4-diethylaminoselenet-2*(*2*H)-*imine* (**7c**). From 0.36 g (2.6 mmol) of **6** and 0.60 g (2.8 mmol) of 4-chlorophenyl isoselenocyanate (**1c**): 0.50 g (54.3%). Yellowish crystals; mp 103-103.5°C (AcOEt/pet. ether/MeOH). IR: 3444*w*, 2973*m*, 2931*m*, 1698*s*, 1620*s*, 1573*s*, 1482*s*, 1445*m*, 1393*s*, 1364*m*, 1320*m*, 1259*m*, 1190*m*, 1161*m*, 1139*w*, 1009*m*. ^{1}H-NMR: 7.29, 6.95 (*AA'BB'*, *J* = 8.7, 4 arom. H); 4.30, 4.35 (2 br *s*, 2 CH_2N); 2.47 (*s*, MeCO); 1.31 (*t*, *J* = 7.1, 2 Me). ^{13}C-NMR: 186.1 (*s*, CO); 161.1, 148.0, 140.2, 130.5, 112.5 (5*s*, 2 arom. C, C(2), C(3), C(4)); 129.2, 122.4 (2*d*, 4 arom. CH); 53.3, 49.6 (2 br, 2 CH_2N); 31.2 (*q*, *Me*CO); 14.2 (*q*, 2 Me). CI-MS: 357 (100, $[M+1]^+$). Anal. Calcd for $C_{15}H_{17}N_2OClSe$: C, 50.65; H, 4.82; N, 7.88. Found: C, 50.70; H, 4.91; N, 7.85.

3-Acetyl-4-diethylamino-N-*(4-methoxyphenyl)selenet-2(2*H)-*imine* (**7d**). From 0.38 g (2.7 mmol) of **6** and 0.60 g (2.8 mmol) of 4-methoxyphenyl isoselenocyanate (**1d**): 0.24 g (25%). Yellow glue. After chromatography (SiO_2, AcOEt/hexane = 1:3), a yellowish glue was obtained, which was directly used for the reaction with morpholine.

Reaction of selenet-2(2*H*)-imines (7) with amines. General Procedure. To a stirred solution of **7** in THF, 1.1-2.0 equivalent of morpholine and cyclohexylamine, respectively, were added. The mixture was stirred for 30 min under reflux. Then, the solvent was evaporated to dryness, and the residue was treated with Et_2O to give yellow crystals.

N,N-*Diethyl-2-[(morpholin-1-yl)(phenylamino)methylene]-3-oxobutane selenamide* (**8a**). From 0.3 g (0.93 mmol) of **7a** and morpholine: 0.18 g (47.3%). Yellow crystals; mp 153-156°C (Et_2O). IR: 3442*m*, 3246*m*, 3193*m*, 3072*m*, 2961*m*, 2923*m*, 2851*m*, 1604*m*, 1546*s*, 1491*s*, 1452*s*, 1416*s*, 1359*s*, 1316*s*, 1294*s*, 1262*s*, 1236*s*, 1214*s*, 1190*w*, 1163*m*, 1130*m*, 1112*s*, 1065*m*, 1021*m*, 1007*m*. ^{1}H-NMR: 10.01 (br *s*, NH); 7.80-6.90 (*m*, 5 arom. H); 4.10-2.00 (*m*, 6 CH_2); 2.10 (*s*, MeCO); 1.30 (*t*-like, 2 Me). CI-MS: 410 (100, $[M+1]^+$). Anal. Calcd for $C_{19}H_{27}N_3O_2Se$: C, 55.88; H, 6.66; N, 10.29. Found: C, 55.39; H, 6.64; N, 10.13.

2-{[(4-Bromophenyl)amino](morpholin-1-yl)methylene}-N,N-*diethyl-3-oxobutane selenamide* (**8b**). From: 0.02 g (0.05 mmol) of **7b** and morpholine: 0.02 g (75.0%). Yellow crystals; mp 178-185°C (Et_2O). IR: 3427*m* (br), 3083*w*, 2967*m*, 2915*m*, 2897*m*, 2852*m*, 1607*s*, 1586*m*, 1536*s*, 1486*s*, 1453*s*, 1405*m*, 1367*s*, 1346*s*, 1285*s*, 1269*s*, 1258*s*, 1239*s*, 1188*m*, 1171*m*, 1141*m*, 1116*s*, 1089*m*, 1078*m*, 1070*m*. ^{1}H-NMR: 14.48 (*s*, OH); 7.71, 7.42 (*AA'BB'*, *J* = 8.8, 4 arom. H); 4.07-3.44 (*m*, 6 CH_2); 1.88 (s, MeCO); 1.43, 1.28 (2*t*, *J* = 7.2, 2 Me). ^{13}C-NMR: 183.7 (*s*, CO); 182.5 (*s*, CSe); 174.5, 140.2, 117.9, 108.9 (4*s*, 2 arom. C, C(2), C(1')); 131.2, 126.0 (2*d*, 4 arom. CH); 54.5, 50.0 (2 br, 2 CH_2N); 48.0 (*t*, 2 CH_2); 45.4 (*t*, 2 CH_2); 26.8 (*q*, *Me*CO); 13.9, 11.7 (2*q*, 2 Me). CI-MS: 488 (91, $[M+1]^+$). Anal. Calcd for $C_{19}H_{26}N_3O_2BrSe$: C, 46.83; H, 5.38; N, 8.62. Found: C, 46.77; H, 5.60; N, 8.50.

N,N-*Diethyl-2-{[(4-methoxyphenyl)amino](morpholin-1-yl)methylene}-3-oxobutane selenamide* (**8d**). After treating the crude of **7d** with excess of morpholine, 0.35 g (30%) of **8d** were obtained. When the chromatographically purified **7d** was treated with morpholine, 17.6% of **8d**

(with respect to **6**) were obtained. Yellow crystals; mp 177-178°C (Et_2O). IR: 3442*m*, 2970*s*, 2924*s*, 2854*s*, 1603*s*, 1536*s*, 1454*s*, 1371*s*, 1349*s*, 1295*s*, 1271*s*, 1257*s*, 1237*s*, 1188*m*, 1173*s*, 1141*m*, 1114*s*, 1089*m*, 1064*m*, 1030*m*. ^{1}H-NMR: 14.17 (*s*, OH); 7.59, 6.87 (*AA'BB'*, *J* = 9.0, 4 arom. H); 3.80 (*s*, MeO); 4.20-3.42 (*m*, 6 CH_2); 1.89 (*s*, MeCO); 1.43, 1.28 (2*t*, *J* = 7.2, 2 Me). ^{13}C-NMR: 183.7 (*s*, CO); 182.0 (*s*, CSe); 174.5, 157.2, 134.3, 108.1 (4*s*, 2 arom. C, C(2), C(1')); 126.3, 113.6 (2*t*, 4 arom. CH); 55.4 (*q*, MeO); 54.6, 50.1 (2 br, 2 CH_2N); 48.0 (*t*, 2 CH_2); 45.4 (*t*, 2 CH_2); 26.6 (*q*, *Me*CO); 13.9, 11.7 (2*q*, 2 Me). CI-MS: 440 (100, $[M+1]^+$). Anal. Calcd for $C_{20}H_{29}N_3O_3Se$: C, 54.79; H, 6.67; N, 9.58. Found: C, 54.43; H, 6.74; N, 9.39.

2-[(Cyclohexylamino)(phenylamino)methylene]-N,N-*diethyl-3-oxobutane selenamide* (**9a**). From 0.31 g (0.96 mmol) of **7a** and cyclohexylamine: 0.12 g (30.0%). Yellow crystals; mp 173-174°C (Et_2O). IR: 3444*m*, 3263*m*, 3176*m*, 2971*m*, 2932*m*, 2855*s*, 1600*s*, 1569*s*, 1505*s*, 1448*s*, 1376*s*, 1351*m*, 1287*s*, 1263*m*, 1247*m*, 1205*m*, 1184*m*, 1152*m*, 1137*m*, 1097*m*. ^{1}H-NMR: 14.64 (*s,* OH); 7.84 (*d*, *J* = 7.6, 2 arom. H); 7.40-7.20 (*m*, 2 arom. H); 7.28 (*t*-like, 1 arom. H); 5.71 (*d*, *J* = 8.2, NH); 4.00-3.80 (*m*, CH_2); 3.60-3.40 (*m*, CH_2, 1 H of cyclohexyl); 2.70-2.40 (*m*, 1 H of cyclohexyl); 1.86 (*s*, MeCO); 1.80-1.60 (*m*, 3 H of cyclohexyl); 1.60-1.05 (*m* with 2*t* at 1.40, 29, 2 Me, 6 H of cyclohexyl). ^{13}C-NMR: 182.3 (*s*, CO); 179.5 (*s*, CSe); 166.3, 141.6, 105.4 (3*s*, 1 arom. C, C(2), C(1')); 128.2, 124.7, 124.3 (3*d*, 5 arom. CH); 55.4 (*d*, CH of cyclohexyl); 47.6, 42.0 (2*t*, 2 CH_2N); 34.1, 33.8 (2*t*, 2 CH_2); 26.8 (*q*, *Me*CO); 25.2, 24.7 (2*t*, 2 CH_2); 13.4, 10.1 (2*q*, 2 Me). CI-MS: 422 (8, $[M+1]^+$, 342 (100). Anal. Calcd for $C_{21}H_{31}N_3OSe$: C, 59.99; H, 7.43; N, 9.99. Found: C, 59.77; H, 7.48; N, 9.87.

2-{[(4-Bromophenyl)amino](cyclohexylamino)methylene}-N,N-*diethyl-3-oxobutane selenamide* (**9b**). From 0.12 g (0.30 mmol) of **7b** and cyclohexyl amine: 0.09 g (64.3%). Yellow crystals; mp 160-173°C (Et_2O). IR: 3420*m*, 3240*m*, 3158*m*, 3096*m*, 3045*w*, 2973*m*, 2931*s*, 2855*s*, 1594*s*, 1548*s*, 1505*s*, 1482*s*, 1449*m*, 1400*m*, 1373*s*, 1350*s*, 1315*m*, 1279*s*, 1264*m*, 1186*m*, 1155*m*, 1139*m*. ^{1}H-NMR: 14.68 (*s*, OH); 7.78, 7.40 (*AA'BB'*, *J* = 8.8, 4 arom. H); 5.57 (*d*, *J* = 8.4, NH); 4.00-3.70 (*m*, CH_2); 3.60-3.30 (*m*, CH_2, 1 H of cyclohexyl); 2.70-2.30 (*m*, 1*H* of cyclohexyl); 1.86 (*s*, MeCO); 1.80-1.60 (*m*, 3 H of cyclohexyl); 1.50-1.10 (*m* with 2*t* at 1.42, 1.30, 2 Me, 6 H of cyclohexyl). ^{13}C-NMR: 182.3 (*s*, CO); 179.9 (*s*, CSe); 166.2, 140.7, 117.4, 105.6 (4*s*, 2 arom. C, C(2), C(1')); 131.1, 125.7 (2*d*, 4 arom. CH); 55.4 (*d*, CH of cyclohexyl); 47.7, 42.0 (2*t*, 2

CH_2N); 34.2, 33.8 (2*t*, 2 CH_2); 26.7 (*q*, *Me*CO); 25.1, 24.7 (2*t*, 2 CH_2); 13.4, 10.0 (2*q*, Me). CI-MS: 502 (4), 500 (6, $[M+1]^+$), 420 (73), 418 (66), 313 (98), 311 (100). Anal. Calcd for $C_{21}H_{30}N_3OBrSe$: C, 50.51; H, 6.06; N, 8.42. Found: C, 50.82: H, 6.29; N, 8.02.

X-Ray Crystal-Structure Determination of **7b** (see *Table 1* and *Figure 1*).[13] All measurements were made on a *Nonius KappaCCD* diffractometer[18] using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an *Oxford Cryosystems Cryostream 700* cooler. The data collection and refinement parameters are given in *Table 1* and a view of the molecule is shown in *Figure 1*. Data reduction was performed with *HKL Denzo* and *Scalepack*.[15] The intensities were corrected for *Lorentz* and polarization effects, and an absorption correction based on the multi-scan method[16] was applied. The structure was solved by direct methods using SIR92,[17] which revealed the positions of all non-hydrogen atoms. One of the N-ethyl groups is disordered over two conformations. Two positions were defined for the atoms of this group and the site occupation factor of the major conformaton refined to 0.709(6). Similarity restraints were applied to the chemically equivalent bond lengths of the disordered region. Neighboring atoms within and between each conformation of the disordered group were also restrained to have similar atomic displacement parameters. The non-hydrogen atoms were refined anisotropically. All of the H-atoms were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2U_{eq} of its parent C-atom (1.5U_{eq} for the methyl groups). Refinement of the structure was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was applied. Neutral atom scattering factors for non-hydrogen atoms were taken from ref.[18], and the scattering factors for H-atoms were taken from ref.[19] Anomalous dispersion effects were included in F_c;[20] the values for *f'* and *f"* were those of ref.[18b] The values of the mass attenuation coefficients are those of ref.[18c] All calculations were performed using *SHELXL97*.[21]

ACKNOWLEDGMENTS

We thank the analytical sections of our institute for spectra and analyses. Financial support of the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, is gratefully acknowledged.

Table 1. *Crystallographic Data of Compound* (**7b**)

Crystallized from		AcOEt/CH_2Cl_2/pet. ether/Et_2O/MeOH
Empirical formula		$C_{15}H_{17}N_2OBrSe$
Formula weight [g mol^{-1}]		400.12
Crystal color, habit		yellow, prism
Crystal dimensions [mm]		0.20 × 0.22 × 0.30
Temperature [K]		160(1)
Crystal system		triclinic
Space group		$P\bar{1}$
Z		2
Reflections for cell determination		18750
2θ range for cell determination [°]		4 – 60
Unit cell parameters:	a [Å]	7.6710(1)
	b [Å]	9.9576(2)
	c [Å]	12.0856(2)
	α [°]	105.7377(7)
	β [°]	94.8258(8)
	γ [°]	112.0784(9)
	V [Å^3]	805.28(2)
D_X [g cm^{-3}]		1.650
μ(MoK_α) [mm^{-1}]		4.816
Scan type		ϕ and ω
2θ(max) [°]		60
Transmission factors (min, max)		0.328; 0.400
Total reflections measured		21000
Symmetry independent reflections		4675
Reflections with $I > 2\sigma(I)$		3859
Reflections used in refinement		4675
Parameters refined; restraints		205; 39
Final: $R(F)$ [$I>2\sigma(I)$ reflections]		0.0301
$wR(F^2)$ (all data)		0.0734
Weights: $w = [\sigma^2(F_o^2) + (0.0304P)^2 + 0.5172P]^{-1}$ where $P = (F_o^2 + 2F_c^2)/3$		
Goodness of fit		1.026
Secondary extinction coefficient		0.014(1)
Final Δ_{max}/σ		0.001
$\Delta\rho$ (max; min) [e Å^{-3}]		0.56; -0.69

REFERENCES AND NOTES

1. "Comprehensive Heterocyclic Chemistry II", Vols. 1-11; ed. by A. R. Katritzky, C. W. Rees, and E. F. V. Scriven, Pergamon Pess, New York, 1996; "Organoselenium Chemistry. Modern Developments in Organic Synthesis", ed. by T. Wirth, Springer Verlag, Berlin, Heidelberg, 2000; H. Ishihara, M. Koketsu, Y. Fukuta, and F. Nada, *J. Am. Chem. Soc.*, 2001, **123**, 8408.
2. M. Koketsu, H. Ishihara, and M. Hatsu, *Res. Commun. Mol. Pathol. Pharmacol.*, 1998, **101**, 179; M. Koketsu, H. Ishihara, W. Wu, K. Murakami, and I. Saiki, *Eur. J. Pharm. Sci.,* 1999, **9**, 157; W. Wu, K. Murakami, M. Koketsu, Y. Yamada, and I. Saiki, *Anticancer Res.*, 1999, **19**, 5375; S. I. Cho, M. Koketsu, H. Ishihara, M. Matsushita, A. C. Nairn, H. Fukazawa, and Y. Uehara, *Biochim. Biophys. Acta*, 2000, **1475**, 207; M. Koketsu, S. Y. Choi, H. Ishihara, B. O. Lim, H. Kim, and S. Y. Kim, *Chempharm. Bull.*, 2002, **50**, 1594.
3. P. K. Atanassov, A. Linden, and H. Heimgartner, *Heterocycles*, 2003, **60**, submitted.
4. P. K. Atanassov, A. Linden, and H. Heimgartner, *Helv. Chim. Acta*, 2003, **86**, in press.
5. a) Y. Zhou and H. Heimgartner, *Helv. Chim. Acta*, 2000, **83**, 539; b) Y. Zhou, A. Linden, and H. Heimgartner, *ibid.*, 2000, **83**, 1576.
6. P. K. Atanassov, A. Linden, and H. Heimgartner, *Helv. Chim. Acta*, in preparation; cf. *Chimia*, 2002, **56**, 358.
7. C. Y. Yoo, E. B. Choi, and C. S. Pak, *Synlett*, 2001, 361.
8. C. K. Johnson, *ORTEPII*, Report ORNL-5138; Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1976.
9. D. H. R. Barton, S. I. Parekh, M. Tajbakhsh, E. A. Theodorakis, and C.-L. Tse, *Tetrahedron,* 1994, **50**, 639.
10. A. Rosowski, R. A. Forsch, and S. F. Queener, *J. Med. Chem.*, 1995, **38**, 2615.
11. R. Leardini, D. Nanni, and G. Zanardi, *J. Org. Chem.*, 2000, **65**, 2763.
12. U. Lienhard, H.-P. Fahrni, and M. Neuenschwander, *Helv. Chim. Acta,* 1978, **61**, 1609.
13. CCDC-215350 contains the supplementary crystallographic data for compound **7b**. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving/html (or from Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U. K. (fax: +44-(0)1223-336033; e-mail: deposit@ccdc.cam.ac.uk).
14. R. Hooft, *KappaCCD Collect Software*, Nonius BV, Deft, The Netherlands, 1999.

15. Z. Otwinowski and W. Minor in *Methods in Ezymology*, Vol. 276, *Macromolecular Crystallography*, Part A, ed. by C. W. Carter, Jr. and R. M. Sweet, Academic Press, New York, 1997, p. 307.
16. R. H. Blessing, *Acta Crystallogr., Sect. A*, 1995, **51**, 33.
17. A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, and M. Camalli, *SIR92*, *J. Appl. Crystallogr.*, 1994, **27**, 435.
18. a) E. N. Maslen, A. G. Fox, and M. A. O'Keefe in *International Tables for Crystallography*, ed. by A. J. C. Wilson, Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 6.1.1.1, p. 477; b) D. C. Creagh and W. J. McAuley, *ibid.*, Table 4.2.6.8, p. 219; c) D. C. Creagh and J. H. Hubbel, *ibid.*, Table 4.2.4.3, p. 200.
19. R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 1965, **42**, 3175.
20. J. A. Ibers and W. C. Hamilton, *Acta Crystallogr.*, 1964, **17**, 781.
21. G. M. Sheldrick, *SHELXL97*, Program for the Refinement of Crystal Structures, University of Göttingen, Germany, 1997.